

Amendments to the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1 - 2 (canceled).

Claim 3 (currently amended): A method of domain specific gene evolution, **the method comprising a first iteration of:**

- a) contacting a target nucleic acid encoding a polypeptide of interest with a recombinase and a first pair of single stranded-targeting polynucleotides which are substantially complementary to each other, wherein each said targeting polynucleotide comprises a homology clamp that substantially corresponds to or is substantially complementary to a first predetermined sequence of said **target** nucleic acid, **said first predetermined sequence** encoding a first domain of said polypeptide, to form a **first recombination intermediate at said first predetermined sequence;**
- b) contacting said **recombination intermediate target** with a single strand-specific nuclease to form a nicked target nucleic acid; and
- c) reassembling and recombining said nicked **or** target nucleic acid to evolve a **first** library of altered target nucleic acids whereby said first predetermined sequence undergoes domain specific gene evolution.

Claim 4 (currently amended): A method according to claim 3 **or** **claim 36,** further comprising:

[[d]] contacting the said target nucleic acid or said first library of altered target nucleic acids of at least one iteration of steps (a) - (c) with a second pair of single-stranded targeting polynucleotides which are substantially complementary to each other and are not substantially complementary to said first pair of **targeting**

polynucleotides, wherein each targeting polynucleotide of said second pair comprises a homology clamp that substantially corresponds to or is substantially complementary to a second predetermined sequence of said target nucleic acid, said second predetermined sequence encoding a second domain of said polypeptide, to form a **second** recombination intermediate at said second predetermined sequence,

whereby said second as well as said first predetermined sequence undergoes domain specific gene evolution.

Claims 5 - 9 (canceled).

Claim 10 (currently amended): A method according to any one of claims 3[[],] or 4, further comprising introducing the resultant product library of altered target nucleic acids resulting from the final iteration of steps (a) - (c) into cells to form a cellular library comprising variant altered nucleic acid sequences.

Claim 11 (previously presented): A method according to claim 10 further comprising expressing said cellular library of altered target nucleic acids to generate a library of variant polypeptides.

Claims 12 - 13 (canceled).

Claim 14 (previously presented): A method according to claim 11 further comprising secreting said cellular library of variant polypeptides.

Claim 15 (canceled).

Claim 16 (previously presented): A method according to claim 29 wherein said cell is eukaryotic.

Claim 17 (previously presented): A method according to claim 29 wherein said cell is prokaryotic.

Claims 18 - 28 (canceled).

Claim 29 (previously presented): A method according to either of claims ~~claim 3[1,] or 4, or 26,~~ further comprising contacting said ~~first~~ recombination intermediate ~~or said second recombination intermediate~~ with a recombination proficient cell.

Claims 30 - 35 (canceled).

Claim 36 (new): The method of claim 3, further comprising:
d) at least one further iteration of steps (a) - (c), with the library of altered target nucleic acids evolved in step (c) of each iteration serving as the target nucleic acid in step (a) of the next successive iteration.

Claim 37 (new). A method of evolving a plurality of domains of a target nucleic acid encoding a polypeptide sequence of interest, the method comprising at least two iterations of:

a) contacting the target nucleic acid with a recombinase and with at least a first and a second plurality of pairs of single-stranded-targeting polynucleotides, wherein each targeting polynucleotide of said first plurality comprises a homology clamp that substantially corresponds to or is substantially complementary to a first predetermined sequence of said target nucleic acid, the first predetermined sequence encoding a first domain of a polypeptide, wherein the targeting polynucleotides of said

first plurality collectively comprise a plurality of sequence mismatches with said first predetermined target sequence;

wherein each targeting polynucleotide of said second plurality comprises a homology clamp that substantially corresponds to or is substantially complementary to a second predetermined sequence of said target nucleic acid, the second predetermined sequence encoding a second domain of said polypeptide, wherein the targeting polynucleotides of said second plurality collectively comprise a plurality of sequence mismatches with said second predetermined target sequence; and

b) introducing said target nucleic acid into a recombination proficient cell to evolve a library of altered target nucleic acids whereby said first and second predetermined sequences undergo domain specific gene evolution,

wherein the library of altered target nucleic acids evolved in step (b) of each iteration serves as the target nucleic acid in step (a) of the next successive iteration of the method.

Claim 38 (new). The method of claim 37, wherein said cell is eukaryotic.

Claim 39 (new). The method of claim 37, wherein said cell is prokaryotic.

Claim 40 (new): The method of any one of claims 37 - 39, further comprising expressing the library of altered target nucleic acids resulting from step (b) of any iteration of the method to generate a library of variant polypeptides.

Claim 41 (new): The method according to claim 40, further comprising secreting said library of variant polypeptides.